REMARKS

In response to the Office Action mailed April 21, 2006, Applicants have amended claim 8. It is urged that support for the above amendment may be found throughout the specification of priority application No. 09/221,107 as originally filed, for example at page 24, lines 18-19. No new matter has been added. The above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Following the amendments, claims 8 and 12-16 are pending in the application. Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks.

Priority

The Action alleges that the prior issued patents or applications to which the present application claims priority do not provide adequate support for administering a patient an antibody or for stimulating an immune response by administering a patient an antibody or antigen-binding fragment. Accordingly, the Action accords the priority date of 11/30/2001 to the claimed invention.

Applicants respectfully traverse the determination of priority on the following grounds. Applicants note that "The claimed subject matter need not be described in *haec verba* to satisfy the written description requirement. The application need not describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that applicant invented the subject matter including such limitations". (*In re Herschler, 591 F.2d 693, 200 U.S.P.Q. 711, 717 (C.C.P.A. 1979)*. Moreover, Applicants submit that this standard is specifically indicated by the U.S.P.T.O. in the Written Description Guidelines (see *Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, para. 1, "Written Description" Requirement* - Federal Register: January 5, 2001 (Volume 66, No. 4, pgs. 1099-1111). For example, the Guidelines state at page 1106, first column:

> If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met (emphasis added).

As such, Applicants submit that the skilled artisan would readily appreciate in view of the disclosure of priority document US non-provisional application 09/221,107 ('107) filed 12/22/1998, as discussed in Applicants' response filed 2/21/2006, that Applicants were in possession of the claimed invention at the time the '107 application was filed.

Notwithstanding the above remarks, without acquiescing to the rejection, and solely to expedite prosecution, Applicants have amended claim 8 to recite "A method for diminishing or eliminating a lung tumor in a patient...". Support for this amendment can be found throughout the '107 specification as filed, for example, at page 24, lines 18-19.

Concerning the allegation that the '107 specification does not provide support for "administering a patient an antibody", Applicants respectfully direct the Examiner to page 27, lines 15-17 of the '107 specification, which reads:

> A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor.

In view of the above remarks, Applicants submit that the presently claimed invention is entitled to the priority date of the filing date of the '107 application, or 12/22/1998. Reconsideration is respectfully requested.

Claim rejections under 35 U.S.C. § 102(b)

Claims 8 and 12 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Holroyd *et al.* (WO 99/44620, publication date 9/10/1999) as evidenced by Abbas *et al.* (page 393, column 2, section antibodies, Cellular and Molecular Immunology, 4th edition, published by W.B. Saunders Co., 2000). In particular, the Action contends that Holroyd *et al.* discloses pharmaceutical compositions comprising an antibody to a protein that is 99.6%

identical to the recited protein set forth in SEQ ID NO:161 and methods of using same for treatment. In view of the teachings of Abbas *et al.*, the Action concludes that the present invention is anticipated.

Applicants respectfully traverse the rejection and submit that since the presently claimed invention is entitled to the priority date of 12/22/1998 (see the remarks regarding priority), the Holroyd *et al.* reference is not prior art under 35 U.S.C. § 102(b). Abbas *et al.* teaches only generally about antibodies. As such, this reference does not anticipate the claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim rejections under 35 U.S.C. § 102(e)

Claims 8 and 12 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Holroyd *et al.* (US Patent 6,576,434) or Pauli *et al.* (US Patent 6,309,857) as evidenced by Abbas *et al.* (page 393, column 2, section antibodies, Cellular and Molecular Immunology, 4th edition, published by W.B. Saunders Co., 2000). The Action reiterates the allegations outlined in the Office Action dated 11/18/2005. In particular, the Action contends that Holroyd *et al.* discloses pharmaceutical compositions comprising an antibody to a protein that is 99.6% identical to the recited protein set forth in SEQ ID NO:161 and methods of using same for treatment. Further, the Action contends that Pauli *et al.* discloses a pharmaceutical composition comprising an antibody to a protein specifically expressed in lung, that is 99.7% identical to the protein set forth in SEQ ID NO:161. The Action additionally asserts that Pauli discloses a method for preventing lung-metastatic tumor spreading by administering such an antibody. In view of the teachings of Abbas *et al.*, the Action concludes that the present invention is anticipated.

Applicants respectfully traverse the rejection on the following grounds. In view of the remarks regarding priority of the claimed invention, Applicants submit that the Holroyd et al. patent cannot be used as prior art against the present invention under 35 U.S.C. § 102(e). In particular, Holroyd et al. is a US Patent of an International Application that was filed before November 29, 2000. Under MPEP 706.02(f)(1)(C)(3)(a), the 102(e) date of an International Application that was filed before November 29, 2000 is the date of entry into the US national stage (§ 371(c)(1), (2), (4) date). For Holroyd *et al.*, this date is February 13, 2001 (not March 3,

1999 as alleged by the Action). Accordingly, since the priority date of the present invention is 12/22/1998, this reference is not prior art to the present invention. Withdrawal of the rejection is respectfully requested.

Concerning Pauli et al., the Action appears to have ignored Applicants' arguments set forth in their response filed February 21, 2006. As noted in that response, Applicants submit that the teachings set forth in this reference do not in any way anticipate the presently claimed invention. In particular, Pauli *et al.* teaches the identification of nucleotide sequences encoding mammalian calcium activated chloride channel-adhesion molecules. One of these molecules (*e.g.*, SEQ ID NO:32) has 99.7% identity to the recited protein of SEQ ID NO:161. The Action alleges that Pauli *et al.* teaches that this similar sequence is specifically expressed in lung. In fact, Pauli *et al.* teaches at Column 14, lines 27-32 that the hCLCA2 mRNA was not detected in lung by Northern blot hybridization. This sequence was detected in lung, trachea and mammary gland using RT-PCR, a more sensitive technique. Thus, the authors conclude that this "[suggests] a significantly lower expression level in the lung."

The Action also contends that Pauli *et al.* discloses using an antibody to the hCLCA2 protein to prevent lung-metastatic tumor spreading. Applicants respectfully disagree with the Action's interpretation of the teachings of Pauli *et al.* The cited reference describes using bovine recombinant and wild-type Lu-ECAM-1 in a cell adhesion assay to test adhesion of the bovine molecules to the murine B16-F10 metastatic melanoma cell line (Column 18, lines 31-41). In this experiment, recombinant bovine Lu-ECAM-1 was better able to adhere to the murine metastatic melanoma cell line than the wild-type bovine Lu-ECAM-1. The interaction of wt-Lu-ECAM-1 was almost completely blocked by an antibody specific for the bovine Lu-ECAM-1. This antibody only partially blocked the recombinant bovine Lu-ECAM-1 interaction. From this experiment, the authors speculate by way of a prophetic example (Example 9, cited by the Action) that administering an antibody raised against bovine Lu-ECAM-1 can be used to block "lung-metastatic" tumor cells ("lung-metastatic" tumor cells meaning melanoma cells that have metastasized to the lung). SEQ ID NO:32, the sequence disclosed by Pauli *et al.* that has the highest identity to the presently recited SEQ ID NO:161, has only 63.7% identity to the bovine Lu-ECAM-1 protein (see Table 2, first row, last column).

Further, there is simply no teaching by Pauli *et al.* that the monoclonal antibody specific for the bovine Lu-ECAM-1 protein used in the adhesion experiments binds to any of the human sequences, let alone one that has only 63.7% identity to the bovine protein and no indication that this antibody can block adhesion of cells expressing the human protein of SEQ ID NO:32 (or the presently recited protein of SEQ ID NO:161) to even metastatic melanoma cells. Thus, Pauli *et al.*, as outlined above, teaches nothing regarding the expression of the protein set forth in SEQ ID NO:161, or even similar proteins, in lung cancer as compared to normal lung tissue nor does this reference teach the use of antibodies specific for the protein of SEQ ID NO:161 for diminishing or eliminating lung tumors. The general antibody teaching of Abbas *et al.* do not remedy the shortcomings of Pauli *et al.* Accordingly, Applicants submit that the cited references do not anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim rejections under 35 U.S.C. § 103

Claims 8 and 12-16 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Holroyd *et al.* (WO 99/44620, publication date 9/10/1999) or Pauli *et al.* (US Patent 6,309,857) as evidenced by Abbas *et al.* (page 393, column 2, section antibodies, Cellular and Molecular Immunology, 4th edition, published by W.B. Saunders Co., 2000) and Brown et al. (US Patent 5,459,043). In particular, the Action contends that the skilled artisan would have been motivated to combine these references with a reasonable expectation of success because Holroyd *et al.* or Pauli *et al.* have shown antibodies which could bind to a protein having high percentage of amino acid identity to the polypeptide of SEQ ID NO:161. Thus, the Action asserts that it would have been *prima facie* obvious to the skilled artisan to arrive at the claimed invention given the teachings of Holroyd *et al.*, or Pauli *et al.*, in view of the general teachings of Abbas *et al.* and Brown *et al.*

Applicants respectfully traverse these grounds for rejection and submit that the cited references, taken alone or for what they teach as a whole, do not obviate the claimed invention. In particular, as noted above, the Holroyd *et al.* reference is not prior art to the claimed invention. Further, as detailed above in relation to the rejections under 35 U.S.C. § 102, there is simply no teaching by Pauli *et al.* that the monoclonal antibody specific for the bovine

Lu-ECAM-1 protein used in the adhesion experiments described therein binds to any of the human sequences, let alone one that has only 63.7% identity to the bovine protein and no indication that this antibody can block adhesion of cells expressing the human protein of SEQ ID NO:32 (or the presently recited protein of SEQ ID NO:161) to even metastatic melanoma cells. Thus, Pauli *et al.* teaches nothing regarding the expression of the protein set forth in SEQ ID NO:161, or even similar proteins, in lung cancer as compared to normal lung tissue nor does this reference teach the use of antibodies specific for the protein of SEQ ID NO:161 for diminishing or eliminating lung tumors. Accordingly, given the shortcomings of the teachings of Pauli *et al.*, the skilled artisan would have had no motivation to combine this reference with any other reference to arrive at the claimed invention. As such, Applicants submit that the cited reference taken for what they teach as a whole do not obviate the claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all of the claims remaining in the application are now believed to be in condition for allowance. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

Julie A. Urvater, Ph.D., Patent Agent
Registration No. 50,461

JAU:ms

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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